Do patients with pure alexia suffer from a specific word form processing deficit? Evidence from ‘wrods with trasnpsoed letetrs’

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Pure alexia is a rare neurological disorder characterized by severe reading difficulties and the absence of other language related impairment.

The clinical distinct features of the disorder are:

1. **Word-length-effect**
   A pronounced increase in reading time as a function of Word length effect. -Behrmann, Plaut & Nelson, 1998

Pure Alexia
Damage to left Occipito-temporal brain areas – Montant & Behrmann, 2000
Also called the visual word form area. Visual-word processing region of the brain.
Specifically, lesions affecting the paraventricular white matter of the left occipital lobe. – Damasio & Damasio, 1983
capable of compromising both interhemispheric and intrahemispheric visual pathways.
Or the **left inferior temporal and fusinal gyri** - Binder & Mohr, 1992, Leff, Spitsyna, Plant, & Wise, 2006, Pflugshaupt et al., 2009

This brain region is responsible for higher level of visual processing, word recognition, also associated with face perception, representation of complex object features (shapes) and recognition of numbers.

or the **left occipito-temporal sulcus**. - Cohen et al., 2003

The most recent studies linked the Common lesion site found in Pure-alexia with the location of The visual word form area. Suggesting that the cognitive Path-mechanism underlying The disorder might be Associated with processing of Visual word form.
The two major hypotheses underlying the cognitive factors of pure-alexia:

1. **Impaired word form processing.**
   Patients may have lost the ability to encode letters in parallel.
   – Rayner & Johnson, 2005 research study
   Mapping the percept of all the letters in a string onto the visual word form. - Leff et al., 2001 research study
   Experimental evidence in support of this hypothesis computed of tasks intended to increase the necessity of whole word reading, as opposed to LBL.

2. **Impaired encoding of letters on a sub-lexical level.**
   - Arguin & Bub, 1993
   Patients display letter confusion that effects visually similar letters.
   - Patterson & Kay, 1982; Peri, Bartolomeo, & Silveri, 1996.
   Experimental evidence in support of this hypothesis, the fundamental role of letter confusion comes from the observation that the characteristic increase in reading time as a function of word length.
In light of these two hypotheses it becomes unclear whether pure alexia is a deficit in word processing or is it letter confusability dyslexia as suggested by Fiset et al. (2005)?

Investigating a specific word form processing deficit requires experimental study that allow manipulating words while keeping letter information constant. Such as, a study that modifies the order of the letters within words, creating ‘jumbled words’.

The ‘jumbled word effect’ possibly could shed a light on how the brain encodes the position of the letters within words.

-Grainger & Whitney, 2004
Word recognition models:


2. **Relative-position coding.** - Grainger & Whitney 2004

Based on ordered letter pairs labeled ‘open bigrams’, these units are open and code the position of a given letter somewhere left or right of another letter.

```
Forest
Fo  Fr  Fe  Or  Oe  Os  Re  Rs  Rt  Es  Et  St
```
The aim of the present study
To investigate the supposed word form processing deficit of pure alexia in three steps,
1. Replicating the two main findings of Warrington & Shallice 1980 patients exhibit enhanced reading difficulties when words are written in script or only briefly presented.
2. Applying jumbled word paradigm.
3. Include LBL reading of healthy adults by having them read sentences with jumbled words, while recording the eye-movement. -control group
* Two patients (PS, RR) fulfilled the main diagnostic of pure-alexia. They had significant word length effect while reading single noun words in German, in the absence of other language-related impairments.

### Table 1A
Demographic and clinical data of the two patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Handedness</th>
<th>Age in years</th>
<th>Education in years</th>
<th>Aetiology</th>
<th>Time post onset in months</th>
<th>Lesion size in ccm³</th>
<th>Affected brain regions² (exclusively in the left hemisphere)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS</td>
<td>Male</td>
<td>Right</td>
<td>53</td>
<td>13</td>
<td>Ischaemic stroke</td>
<td>13</td>
<td>63.90</td>
<td>Fusiform gyrus; lingual gyrus; inferior temporal gyrus; hippocampus; parahippocampal gyrus; inferior, middle, and superior occipital gyri; calcareous sulcus; cuneus.</td>
</tr>
<tr>
<td>RR</td>
<td>Male</td>
<td>Right</td>
<td>70</td>
<td>13</td>
<td>Haemorrhagic stroke</td>
<td>112</td>
<td>99.00</td>
<td>Fusiform gyrus; lingual gyrus; inferior and middle temporal gyri; parahippocampal gyrus; inferior, middle, and superior occipital gyri; calcareous sulcus; cuneus.</td>
</tr>
</tbody>
</table>

¹ Measured with MIRcroN (www.mricro.com/mricron) on the normalised brain.  
² Based on the Automated Anatomical Labelling (AAL) map (Tzourio-Mazoyer et al., 2002).
### Methods

**Table 1B**

Single letter naming and word-length effect (WLE).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Single letter naming&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Word-length effect (WLE)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean reaction time in ms</td>
<td>t (df = 9)</td>
</tr>
<tr>
<td>PS</td>
<td>780</td>
<td>1.584</td>
</tr>
<tr>
<td>RR</td>
<td>783</td>
<td>1.605</td>
</tr>
</tbody>
</table>

<sup>a</sup> Based on a task during which patients had to name all 26 lowercase letters of the German alphabet – which appeared one-by-one on a notebook screen, to the left of a preceding central fixation point – as accurately and quickly as possible. Letters were written in Arial, font size was 125 pixels, corresponding to 1.4° of visual angle on average. Participants were instructed to press a key as soon as they identify the letter, and to name it aloud thereafter.

<sup>b</sup> One-tailed error probability of a modified t test specifically designed to compare the value of a single patient with those of a small control group (Crawford & Howell, 1998). Values are compared with those of the healthy control group (N = 10; mean = 554 ms, SD = 136 ms).

<sup>c</sup> This task is described in the caption to Fig. 1.

<sup>d</sup> Word-length effect (WLE) in ms per additional letter.

<sup>e</sup> One-tailed error probability of a modified t test specifically designed to compare the value of a single patient with those of a small control group (Crawford & Howell, 1998). Values below 0.05 confirm the hypothesis that the WLE of a given patient is significantly larger than corresponding values from the healthy control group (N = 10; mean = 12 ms, SD = 12 ms).
both patients suffered a stroke in the supply territory of the left posterior cerebral artery, causing brain damage predominantly in the ventral parts of the left occipital and temporal lobe.

Fig. 2. (A) Brain lesions of the two patients with pure alexia. Lesions were marked on T2-weighted MR-scans (FLAIR sequence) using the freely available MRicroN software (www.mricro.com/mricron; Rorden, Karnath, & Bonilha, 2007), then normalised with SPM5 (www.fil.ion.ucl.ac.uk/spm) and plotted on the CH2 template brain in MRicroN. The selection of axial slices corresponds to that of previous studies on pure alexia (Leff et al., 2006; Plugshaupt et al., 2009). White crosshairs show the coordinate assigned to the centre of the VWFA in healthy adults (Jobard et al., 2003). (B) Central visual fields (radius = 30°) of the two patients, based on automated static perimetry. Field defects are highlighted by a superimposed semi-transparent grey area.
Single word reading tasks:

1. Print Vs script reading - 50 German seven letter words nouns were written in Arial script, words were matched with regard to frequency, concreteness, image-ability. Participants had to press a key if they indentify the word, and to read the word aloud.

2. Reading briefly presented words - 30 German five letter nouns and 30 five letter non-words were presented. Participants had to indicate whether a word or non-word were briefly displayed by pressing one or the two predefined keys.

3. Reading jumbled words - 60 German five letter nouns were evenly assigned to three condition; un-jumbled, slightly jumbled, heavily jumbled words. The three condition were matched with regards to frequency, concreteness and image-ability. Participants were asked to identify the ‘base words’ in all conditions.
Reading sentences with jumbled words task

21 standardized German sentences developed by Radner et al. 2002, each sentence started with a main clause followed by a relative clause (14 words in total). Including three conditions; normal letter order, jumbled internal letters, jumbled initial letters. Eye movement during sentence reading was recorded. The participants had to silently read the sentence before stopping it presentation with another button press.
Results

**Single word reading tasks**

Patients needed more time reading words written in script than print. In RR patient the script read deficit concerned accuracy as well. In reading Words Vs non-words task the reading accuracy of both patients was significantly lower than the controls.

The control group found to have had significant main effect on accuracy and reading speed when reading heavily jumbled words as oppose to slightly jumbled words.
# Results

### Table 2

Results of the print versus script reading task.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Condition</th>
<th>PS</th>
<th>RR</th>
<th>Controls’ mean (SD)</th>
<th>t (df = 9)</th>
<th>P (one-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy (%)</td>
<td>Print</td>
<td>100.00</td>
<td>96.00</td>
<td>100.00 (0.00)</td>
<td>-0.303</td>
<td>0.385</td>
</tr>
<tr>
<td></td>
<td>Script</td>
<td>100.00</td>
<td>70.83</td>
<td>99.60 (1.26)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuracy difference (%)</td>
<td>(Print – script)</td>
<td>0.00</td>
<td>25.17</td>
<td>0.40 (1.26)</td>
<td>18.744</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean reaction time (s)</td>
<td>Print</td>
<td>2.756</td>
<td>2.365</td>
<td>0.522 (0.085)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Script</td>
<td>3.189</td>
<td>3.736</td>
<td>0.550 (0.093)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean reaction time difference (s)</td>
<td>(Script – print)</td>
<td>0.434</td>
<td>1.370</td>
<td>0.028 (0.029)</td>
<td>44.122</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Notes:** Reaction time data loss due to responses longer than 20 s was 0% in the control group as well as in PS and 4% in RR. Moreover, reaction times from both correct and incorrect responses were used to calculate mean reaction times per condition.

* One-tailed error probability of a modified t test specifically designed to compare the value of a single patient with those of a small control group (Crawford & Howell, 1998).
### Table 3
Results of the jumbled word reading task.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Condition</th>
<th>PS</th>
<th>RR</th>
<th>Controls' mean (SD)</th>
<th>t (df = 9)</th>
<th>P (one-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy (%)</td>
<td>Normal</td>
<td>100.00</td>
<td>100.00</td>
<td>100.00 (0.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Slightly jumbled</td>
<td>83.33</td>
<td>65.00</td>
<td>93.50 (7.84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heavily jumbled</td>
<td>21.10</td>
<td>25.00</td>
<td>72.50 (12.96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accuracy decrease (%)²</td>
<td></td>
<td>39.47</td>
<td></td>
<td>13.75 (6.48)</td>
<td>3.784</td>
<td>0.002</td>
</tr>
<tr>
<td>Mean reaction time (s)</td>
<td>Normal</td>
<td>2.958</td>
<td>4.293</td>
<td>0.928 (0.179)</td>
<td>2.391</td>
<td>0.020</td>
</tr>
<tr>
<td></td>
<td>Slightly jumbled</td>
<td>8.808</td>
<td>8.768</td>
<td>2.506 (0.744)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heavily jumbled</td>
<td>8.738</td>
<td>11.860</td>
<td>7.370 (1.880)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean reaction time increase (s)³</td>
<td></td>
<td>2.890</td>
<td></td>
<td>3.221 (0.899)</td>
<td>−0.351</td>
<td>0.367</td>
</tr>
</tbody>
</table>

Notes: Reaction time data loss due to responses longer than 20 s was 0% in the control group as well as in RR and 5% in PS. Moreover, reaction times from both correct and incorrect responses were used to calculate mean reaction times per condition.

² Mean decrease in accuracy per 25% reduction in open bigram overlap, which is 100% for normal words, 75% for slightly jumbled words, and 50% for heavily jumbled words.

³ Mean increase in reaction time per 25% reduction in open bigram overlap.

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**Results**
**Sentence reading task**
Both patients exhibit significant comprehension difficulties in sentences containing jumbled words.

Sentences containing target words with initially jumbled letters evoked pure alexia fixation behavior in controls.

Both patients displayed LBL reading in all three conditions, showed significantly enhanced fixation frequencies and partly prolonged fixation durations.

**Results**
### Table 4
Results of the sentence reading task.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Condition</th>
<th>PS</th>
<th>RR</th>
<th>Controls’ mean (SD)</th>
<th>t (df= 9)</th>
<th>P (one-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comprehension accuracy (%)</td>
<td>Normal</td>
<td>95.24</td>
<td>95.24</td>
<td>98.57 (2.30)</td>
<td>-1.380</td>
<td>0.100</td>
</tr>
<tr>
<td></td>
<td>Internal</td>
<td>76.19</td>
<td>55.56</td>
<td>94.76 (6.13)</td>
<td>-2.888</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>61.90</td>
<td>38.10</td>
<td>90.00 (12.18)</td>
<td>-2.200</td>
<td>0.028</td>
</tr>
<tr>
<td>Fixation frequency (fixation-to-character ratio)</td>
<td>Normal</td>
<td>1.64</td>
<td>0.96</td>
<td>0.30 (0.09)</td>
<td>14.019</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Internal</td>
<td>2.81</td>
<td>2.70</td>
<td>0.43 (0.18)</td>
<td>12.989</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>3.19</td>
<td>2.97</td>
<td>0.62 (0.29)</td>
<td>8.338</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean fixation duration (ms)</td>
<td>Normal</td>
<td>303</td>
<td>288</td>
<td>226 (28)</td>
<td>2.653</td>
<td>0.013</td>
</tr>
<tr>
<td></td>
<td>Internal</td>
<td>315</td>
<td>313</td>
<td>247 (27)</td>
<td>2.375</td>
<td>0.021</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>315</td>
<td>318</td>
<td>262 (35)</td>
<td>1.539</td>
<td>0.079</td>
</tr>
</tbody>
</table>

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* a Experimental conditions: normal - all words with normal letter order, internal - the three target words had jumbled internal letters, initial - the three target words had jumbled initial letters.

* b One-tailed error probability of a modified t test (Crawford & Howell, 1998).
Results
The first main finding
During single word reading the accuracy of both patients decreased with the severity of jumble words, and was larger than of controls. This finding supports of word form processing deficit in pure alexia, However, both patients showed minor letter confusion and trend towards prolong RT during single letter reading. Concluding that reading difficulties of both patients are consequence of deficient word form processing and letter discrimination.

The second main finding
It was possible to provoke pure-alexia like reading in healthy adults. (fixation patterns) by jumbling sub-set of words in reading sentence task. The initial condition fixation frequency of controls was similar to normal reading condition of patients, hence, the controls fixation frequency in initial jumbled sentences equaled the LBL reading that is defined feature of pure alexia. Suggesting, once more that impairment in word form processing is associated with pure-alexia.
The third main finding

In examining jumbled word effect, the single word reading task corroborated with Grainger & Whitney 2004 hypothesis, the healthy adults displayed significantly higher bigram overlap with the un-jumbled variant as opposed to heavily jumbled words. This possibly provides evidence for relative encoding of letter position in the brain than precise one.

Concluding, that reading difficulties of both patients are consequence of deficient word form processing and letter discrimination.
* is the letter discrimination is associated with the deficiency in word form processing???

*No clear explanation concerning the jumbled word length effect among both patients compared to controls.

*No significant differences was found among patients in terms of duration of fixation on target words. Could be that letter discrimination effect is less of importance in pure-alexia?.

My own thoughts
Thank You